in a user-friendly environment during a decision-making setting avoiding disadvantages of pre-prepared analyses.

PRM196

AN EVALUATION AND COMPARISON OF METHODS USED IN SURVIVAL ANALYSIS TO FIT DISTRIBUTIONAL CURVES TO KAPLAN-MEIER DATA

Haines P

Curo, Marlow, UK

OBJECTIVES: HTA bodies increasingly require accurate survival estimates in order to provide reliable recommendations. It is argued that access to individual patient data (IPD) can improve their accuracy. This paper aims to assess to what degree extracting IPD from published Kaplan-Meier curves helps improve extrapolated survival estimates. Some methods currently used for HTA submissions fit a survival curve directly to a published Kaplan-Meier curve, but does this lack accuracy? **METHODS:** Two methods used to extract the IPD from Kaplan-Meier curves reviewed in this paper are by Guyot et al (Guyot, Ades, Ouwens, & Welton, 2012) and Hoyle and Henley (Hoyle & Henley, 2011) which were compared against the outcomes of the standard 'least squares' method. Comparisons were made for two situations: 1) when numbers at risk are available at different time points throughout the Kaplan-Meier curve and 2) when numbers at risk are only available at the start. **RESULTS:** The three methods resulted in the long-normal distribution showing the best fit, with all containing the true mean and median within their confidence intervals. However, the Hoyle and Henley method estimates a mean marginally closer to the true mean than the other methods in both situations. When many numbers at risk are provided, the Hoyle and Henley method gives narrower confidence intervals. Both extraction methods slightly outperformed the least squares method. The three methods give median estimates and resulting confidence intervals which are statistically equivalent to that of the IPD, except for the Guyot method when numbers at risk are not available. **CONCLUSIONS:** In conclusion, extraction methods can give marginally better results than the Least Squares method. However, these results may not be applicable to other examples. In addition, the extra time taken to run extraction methods could be too large to account for the small improvement in accuracy of results.

PRM197

MULTI-LEVEL NETWORK META-ANALYSIS TO ACCOUNT FOR DOSE-RESPONSE AND CLASS EFFECTS

Reason T[1], Dias S[2], Welton N[2]

[1]*IMS Health, London, UK,* [2]*University of Bristol, Bristol, UK*

OBJECTIVES: A frequent challenge in Network Meta-Analysis (NMA) arises from the fact that several interventions may belong to the same class and be given at multiple doses. Models have been proposed for NMA accounting for dose-response, but these models do not also consider class effects at the same time, which are important from a decision making perspective. We aim to develop a framework that extends dose-response NMA methods to account for dose and class effects simultaneously, and explore the ability of these models to explain heterogeneity, improve model fit and increase precision of the estimated treatment effects. **METHODS:** Using clinical trial data of treatments for acute migraine obtained from Cochrane reviews, we developed multi-level NMA models to simultaneously account for dose-response and class-effects, in particular defining a 'dose', 'treatment' and 'class' hierarchy within the NMA models. We explored a non-parametric "random walk" model constrained to be monotonically increasing with dose. Multi-level NMA models were compared to 1-level (standard) NMA models where interventions were 'lumped' at each level separately. **RESULTS:** The model that explicitly included monotonic dose-response and class effects showed the best fit and least heterogeneity, and produced more precise measures of treatment effect than all 1-level models. NMA models that made less plausible assumptions around dose-response had poorer fit than models with monotonic dose-response. **CONCLUSIONS:** We have developed a framework for simultaneously estimating treatment effects at the 'dose', 'treatment' and class level within the same NMA model. The framework can help decision makers identify the most appropriate class, drug, and dose, however, results of dose-response models are not straightforward to interpret or implement from a decision making perspective. Careful consideration should be given to dose-response and similarity of interventions when conducting NMA.

PRM198

THE LUMLEY-METHOD, A RECOMMENDED NETWORK META-ANALYSIS FOR INDIRECT COMPARISONS, SUMMARIZED FOR PRACTITIONERS

Petto H[1], Kadziola Z[1], Belger MA[2]

[1]*Eli Lilly Regional Operations GmbH, Vienna, Austria,* [2]*Eli Lilly and Company, Windlesham, UK*

OBJECTIVES: In recent years we have seen a growth in the use of network meta-analysis as part of the evidence base for Health Technology Assessments, with the Lumley method, published in 2002[1]being a key reference when considering both indirect and direct comparisons. Unfortunately the program-code included in the manuscript cannot easily be run, and the given examples cannot be replicated, even with corrected code. To give practitioners helpful insight into the method, we start from individual patient data of head to head trials and show how from subsequent data-aggregation the Lumley-model (a random-effects model) can be derived. **METHODS:** We give more details than in the article of how the proposed variance function aggregates study-heterogeneities and of how effect-sizes and confidence intervals can be derived from the parameter- and variance-estimates. We discuss why dependencies coming from the network-structure should be incorporated into confidence-interval calculations and of how the model can be extended with an in the article suggested Bayesian approach for modeling the random-effects parameters. **RESULTS:** We include an example of how the Lumley-method can be applied in practice. We present based on the program-example in the article a corrected R-version and a translation into SAS. For both we show how aggregated study-data should be structured and dummy-coded before running the program. The Lumley-method was applied to simulated data with known model-parameters and we show for different scenarios how close the estimates come. For selected treatment comparisons we present effect-sizes with confidence intervals. We apply also the Bayesian extension and discuss its advantages. **CONCLUSIONS:** Based on our research we give recommendations of when the Lumley-method should be best applied, and discuss limitations.[1] Lumley T: Network meta-analysis for indirect treatment comparisons. Stat. Med. 2002; 21: 2313-2324.

PRM199

ANALYSIS OF VOLUME AND STRUCTURE OF ORAL ANTIDIABETIC DRUGS CONSUMPTION IN UKRAINE

Iakovlieva L, Kyrychenko O, Gerasymovà O, Kuznetsov I

National University of Pharmacy, Kharkiv, Ukraine

OBJECTIVES: Evaluation and comparison of oral antidiabetic drugs (OAD) consumption at state level are an important element at control of 2ndtype DM patients treatment quality. The objective of the study is to determine the volumes and structure of OAD consumption in Ukraine and to compare it with consumption in the other countries. **METHODS:** ATC/DDD-methodology with application of DDD/1000/day (DID). The evaluation is based on consumption volume, provided by "PharmXplorer/Pharmstandard" analytical system of market research. **RESULTS:** In year 2008, OAD consumption in Ukraine was 5.78 DID and increased to 11.13 DID in year 2013. In year 2011, OAD consumption was 54.28 DID in France, 44.58 - in Germany (S. Pichetti, C. Sermet, S. van der Erf, 2013), 33.25 - in Estonia, 29.87 - in Latvia (Baltic Statistics on Medicines 2010–2012), showing that OAD consumption in Ukraine was very low. Structure of OAD consumption in Ukraine shows that 98.95% of the total consumption volume is distributed to 2 groups: sulfonylureas (73.84%) and biguanides (25%) and only 1,05% to gliptines, glitazones, glucosidases and glinides. The total share of preparations of sulfonylureas and biguanides group in the total consumption structure in France and Germany was 71.8% and 80.1% respectively of the total consumption OAD. In year 2013, OAD of the II generation - gliclazide (3.01 DID) and glibenclamide (2,09 DID) had the highest consumption level in sulfonylureas group, preparations of III generation - glimepiride (2,09 DID) had lesser consumption rate. Out of 61 OAD trade names (TN), presented in the pharmaceutical market of Ukraine, 8 TNs took 89.78% of the total consumption volume. **CONCLUSIONS:** Very low rate of OAD consumption in Ukraine shows the necessity of its increase. Analysis of OAD consumption structure evidences the application of relatively cheap and long-used medical preparations for treatment of 2nd type DM, which is largely due to financial capacities of payers.

PRM200

DEVELOPMENT OF A WEB-BASED TOOL TO ELICIT THE OPINION OF REGIONALLY DISPERSED HEALTH CARE PROFESSIONALS RESPONSIBLE FOR MEDICAL DEVICE VIGILANCE

Pibouleau L[1], Galtier T[1], Sailly AC[2], Maison P[2], Katsahian S[3]

[1]*INSERM, CRC, Paris, France,* [2]*Agence Nationale de Sécurité des Médicaments, Saint-Denis, France,* [3]*Hôpital Européen Georges Pompidou, Paris, France*

OBJECTIVES: In the context of uncertainty due to the lack of sound data, expert opinion is considered as a legitimate source of information for decision-makers. The use of experts' opinion requires to quantifying their uncertainty about a specific event by eliciting a probability distribution of the event. The objectives of this study were to develop a web-based tool enabling users to remotely elicit the opinion of a group of geographically dispersed experts and to evaluate the measurement properties of this tool. **METHODS:** The web-based tool allowed first to elicit univariate probability distributions separately from each expert and secondly to calculate an aggregated distribution. The elicitation method was the four-interval method that was judged to be more appropriate for non-statistician experts due to its clarity of use. As recommended to limit biases, the elicitation questionnaire included a training exercise and a graphical feedback so that the experts could validate their distributions. A pilot survey was conducted among all the French regional medical device vigilance correspondents (n=24) about the risk of failure (%) of an implantable medical device. **RESULTS:** Twenty-two correspondents (92%) completed the survey. An aggregated distribution was calculated from the elicited individual distributions and a beta distribution was fitted reflecting the group uncertainty about the risk of failure. Feasibility was judged in view of the users' feedback and time to completion. Validity and reliability were assessed using data on comprehensiveness, internal coherence and test-retest reliability. **CONCLUSIONS:** The proposed web-based tool was feasible, valid and reliable. It should be useful in making expert elicitation easier and more practical.

PRM201

KNOWLEDGE ON MEDICATION TAKING BEHAVIOUR, BALANCED DIET AND PHYSICAL ACTIVITY - A SURVEY AMONG THE ADOLESCENTS

sandeep Chowdary K, Nallani VRR

Chalapathi Institute of Pharmaceutical Science, Guntur, India

OBJECTIVES: The main objective of the study is to promote awareness and assess the knowledge of adolescents on medication use, importance of balanced diet and physical activity. **METHODS:** The study was conducted among the adolescents aged from16-18 years in Regions of Guntur. The volunteers are allowed to fill their informed consent to be a part of the study. The questionnaire was distributed to all the volunteers included in the study, which includes questions on their medication taking behaviour, dietary habits and physical activity. The response was then analyzed to assess the knowledge on medication use, balanced diet and physical activity. **RESULTS:** Among the 165 individuals on assessment of their medication taking behavior78% of them do not follow their prescription, 61% of the individuals do not have any idea on their medication use and a majority of 74% are not aware of the unwanted effects caused by the medication. On assessment of their dietary habits and physical activity, 62% of the individuals include meal rich in fat, 42% of the individuals skip their breakfast every day and 41% of them will not include leafy vegetables as part of their regular meal. 65% of individuals do not perform a regular physical activity **CONCLUSIONS:** It is the responsibility of the pharmacist

to promote awareness on the medications, balanced diet and physical activity to improve the quality of life of an individual.

PRM202

SIMULATING INDIVIDUAL PATIENT LEVEL DATA TO ADDRESS TREATMENT SWITCHING WHEN ONLY SUMMARY DATA ARE AVAILABLE

Boucher R, Abrams K, Lambert PC
University of Leicester, Leicester, UK

OBJECTIVES: Treatment switching commonly occurs in the pivotal HTA evidence for advanced or metastatic cancer treatments submitted to reimbursement agencies. Simple approaches, such as Intention-to-treat (ITT) analysis, have typically been used to analyse data with treatment switching, despite simulation studies showing these to drastically underestimate the underlying treatment effect. With more manufacturers conducting indirect comparisons (ICs) to compare treatments, summary data are being used more in analysis. The method outlined addresses treatment switching when only summary data are available to ensure appropriate estimates for the treatment effect are achieved when the data is then used in an IC. **METHODS:** Using digitised survival curves, multiple datasets that are representative of the original individual patient data (IPD) are simulated. Treatment switching information is estimated from reported information on progression-free survival, and then established methods which adjust appropriately for treatment switching used to analyse the simulated data. This approach is applied to an example from a technology appraisal (TA) submitted to National Institute for Health and Care Excellence (NICE), and the ITT hazard ratio and median survival obtained and compared with those reported, before analysis using a Rank Preserving Structural Failure Time Model (RPSFTM). **RESULTS:** Averaging over 2000 datasets, the replicated summary statistics were similar to those reported. Both median survival times were within 1 month of those stated in the TA and the hazard ratio less than 0.05 different. Subsequent analysis using an RPSFTM shows the new treatment to be more effective, and inappropriately adjusting for crossover to have underestimated the treatment effect. **CONCLUSIONS:** Adjusting summary data is important as otherwise, subsequent analysis conducted will give inappropriate results. The simulated data approach well represents the original IPD, giving on average similar results to those reported. Hence, the further analysis to address treatment switching issues gives more appropriate treatment effect estimates.

PRM203

MODELING THE EFFECT OF COMBINING ALOGLIPTIN WITH DUAL THERAPY IN TYPE 2 DIABETES

Johnson KI[1], Palin HJ[1], Sibbring GC[1], Selby R[2]
[1]*Complete Clarity, Macclesfield, UK,* [2]*Takeda UK, High Wycombe, UK*

OBJECTIVES: To estimate the impact of combining the dipeptidyl peptidase-4 (DPP-4) inhibitor, alogliptin, with metformin and sulfonylurea (alogliptin triple therapy) to achieve glycemic control in patients with type 2 diabetes. **METHODS:** Since no clinical trial of alogliptin triple therapy has been conducted, the effect of adding alogliptin to dual therapy (metformin+sulfonylurea) was modeled using novel additive effect methodology, utilizing data from a previous mixed treatment comparison (MTC). The following assumptions were made: the efficacy of triple therapy can be estimated as a function of its constituent parts, and the efficacies of the constituent parts are equivalent. Pooled data for the absolute change from baseline in glycosylated hemoglobin (HbA_{1c}) from trials of sitagliptin, linagliptin, and vildagliptin triple therapy, and for their constituent parts, informed the model. A weighting factor, β coefficient, derived from DPP-4 mono, dual, and triple therapy trials, was used to estimate the effect size for triple therapy using the sum of the constituent parts. The estimated mean β value was validated against the observed effect size of alog liptin+pioglitazone+metformin, using the pooled effect from the MTC. **RESULTS:** An estimated mean β coefficient value of 0.83 represented the DPP-4 inhibitor class. Validation of the approach resulted in a similar β coefficient for pioglitazone triple therapy (0.82). Absolute change in HbA_{1c} from baseline for alogliptin triple therapy was estimated as -0.77% (95% CI -1.16, -0.39). Similar values were observed in the MTC for sitagliptin -0.94% (95% CI -7.34,5. 40), linagliptin -0.65 (95% CI -6.87,5. 60), and vildagliptin -0.80% (95% CI -7.00,5. 43). **CONCLUSIONS:** The wide confidence interval is consistent with expectations in the literature and is a limitation of the method employed, in that it requires the variance of the individual studies to be summated. Nevertheless, the method demonstrates the value of modeling when clinical trial evidence is not available.

PRM204

UNCERTAINTY AND PROBABILISTIC METHODS IN MULTI-CRITERIA DECISION ANALYSIS

O Meachair S, Walsh C
Trinity College Dublin, Dublin, Ireland

OBJECTIVES: Multi-Criteria Decision Analysis (MCDA) is a collection of techniques for choosing optimal decisions when two or more criteria need to be taken into account in the decision process. Most MCDA techniques require the specification of a number of parameters; criteria weights, utility functions or indifference thresholds. We wish to account for the uncertainty in these parameters which may arise due to the fuzzy nature of the Decision Maker's preferences, conflicting opinions between a group of decision makers or population group, or the abstract nature of the parameters. **METHODS:** We implement some MCDA models from a Bayesian perspective where parameters come from posterior probability distributions representing the combination of available knowledge on the parameters. Such knowledge can come from empirical data, expert elicitation, survey data, decision-making committees, or some combination of these. **RESULTS:** Depending on the method used, the end result is either a benefit function which quantifies the uncertainty in the benefit score for each action, or a rankogram which depicts the uncertainty in the ranking of actions. **CONCLUSIONS:** Knowledge about this uncertainty allows decision makers to make more informed decisions. A decision action may be clear when uncertainty is sufficiently low, or it may be necessary to request more information or to refine the decision formulation if uncertainty is high, potentially leading to improved decision-making.

PRM205

SYSTEMATIC REVIEW AND CRITICAL APPRAISAL OF THE STATISTICAL METHODS USED IN PUBLISHED STUDIES TO INDIRECTLY COMPARE NOVEL ANTICOAGULANTS (NOACS) WITH WARFARIN FOR THE PREVENTION OF STROKE IN PATIENTS WITH ATRIAL FIBRILLATION (AF)

Daacke IM
Boehringer Ingelheim UK, Bracknell, UK

INTRODUCTION: The three main novel anticoagulants (NOACs) currently licensed in Europe, apixaban, dabigatran and rivaroxaban, have all been directly compared against warfarin in randomised controlled trials. However, none of the three drugs have been directly compared against each other. Thus, there has been an increase in the number of meta-analyses and indirect comparisons published comparing the relative efficacy and safety of these novel anticoagulants against each other via warfarin as a common comparator. **OBJECTIVES:** Systematically review all meta-analyses and indirect comparisons evaluating the NOACs against warfarin for the prevention of stroke in patients with AF and critically appraise the statistical methods used to do so. **METHODS:** Systematic searches of EMBASE, MedLine, EBM Reviews, EconLIT as well as manual searches of ClincalTrials. gov, the Cochrane Library, CADTH, NICE, NHSEED and HTA were conducted. Data was abstracted from any citation applying statistical methods to compare the efficacy and safety of NOACs for the prevention of AF-related stroke. Information regarding the statistical approach; model assumptions; data presentation; interpretation of the evidence; and discussions of internal and external validity was used to quality rate each study. **RESULTS:** Bucher's method of adjusted indirect comparison was most widely used. There were generally three main model assumptions required: the similarity, homogeneity and consistency assumptions, each being investigated with varying scrutiny in the studies reviewed. According to the quality assessment, the indirect comparison conducted by Wells and colleagues (2012) is of the highest relative quality. **CONCLUSIONS:** The limited number of RCTs available comparing the NOACs to standard therapy, creates considerable uncertainty surrounding the comparative efficacy and safety of these anticoagulants. In order to establish which individual NOAC is most likely to benefit a given patient population, indirect comparisons and meta-analyses are increasingly used. However, the quality of indirect comparison studies are variable and results should be interpreted with care.

PRM206

METHODOLOGICAL ASSESSMENT OF MATCHING-ADJUSTED INDIRECT COMPARISONS: CASE STUDY APPLICATION TO ATTENTION DEFICIT/ HYPERACTIVITY DISORDER (ADHD)

Shafrin J[1], Sikirica V[2], Shrestha A[1], Henkhaus LE[3], Erder MH[2], Chandra A[4]
[1]*Precision Health Economics, Los Angeles, CA, USA,* [2]*Shire Development, LLC, Wayne, PA, USA,* [3]*University of Southern California, Los Angeles, CA, USA,* [4]*Harvard University, Cambridge, MA, USA*

OBJECTIVES: Matching-adjusted indirect comparison (MAIC) is a novel comparative effectiveness approach to address biases that can appear in traditional indirect comparison (IC) methods when patient characteristics differ across trials. We examined three unanswered MAIC methodological questions and applied the proposed solutions to a comparison of ADHD treatments. **METHODS:** Using individual patient data from two randomized controlled trials (RCTs) comparing guanfacine (GXR) vs placebo and published summary statistics from four RCTs comparing atomoxetine (ATX) vs placebo, MAIC was used to reweight the GXR data so that observable GXR patient characteristics matched those of ATX patients. Change in ADHD-RS-IV scores was the primary endpoint. Comparative efficacy results were evaluated for their sensitivity to changes in the following three MAIC specifications: variable selection using regression-based methods, statistical moments matched (i.e., mean vs mean and variance), and matching on placebo-arm outcomes. **RESULTS:** Both treatments decreased ADHD-RS-IV scores relative to placebo (-17.9 GXR vs -10.7 placebo; -14.6 ATX vs -5.8 placebo). In the baseline MAIC specification adjusting for patient baseline characteristics and placebo arm outcomes, GXR produced larger decreases in ADHD-RS-IV scores than ATX (Δ: -3.9, $p<0.004$). The results were insensitive to adding variables to the matching algorithm (Δ: -3.8, $p<0.023$), or matching only covariate means rather than both means and variances (Δ: -3.6, $p<0.006$). Applying MAIC without matching placebo arm outcomes indicated a slightly greater decrease in ADHD-RS-IV scores for ATX, but there was no statistically significant difference between GXR and ATX (Δ: 0.6, $p<0.649$). **CONCLUSIONS:** In this study, MAIC results were insensitive to variable selection via regression and the statistical moments matched, but matching the placebo arms altered the results. Matching placebo arm outcomes is valid when unobserved trial-specific factors have a differential impact on a trial's treatment and control arm outcomes; this was likely the case in this GXR-ATX study.

PRM207

PROPOSED CHECKLIST FOR NON-STATISTICIANS TO ASSESS THE QUALITY OF A NETWORK META-ANALYSIS IN THE CONTEXT OF A NICE SUBMISSION

Pacou M[1], Gauthier A[2], Taieb V[2], Bec M[2], Belhadi D[2], Guillemot J[2]
[1]*Amaris, Paris, France,* [2]*Amaris, London, UK*

OBJECTIVES: To develop a checklist to assess the quality of a network meta-analysis (NMA) in the context of a submission to NICE. This checklist is intended to be comprehensible and easy-to-use by non-statisticians to assess whether an NMA is suitable for a submission to NICE and/or to populate cost-effectiveness models within the context of the NICE requirements. **METHODS:** An ad-hoc search of the literature was conducted to identify existing checklists. Items from these checklists were extracted and critically reviewed. Recommendations from NICE as well as existing NICE submissions and corresponding comments from the evidence review groups (ERG) were used to develop the checklist. Our checklist was validated by health economists and pharmacists not trained in NMA on the basis of a NICE submission